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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,886	01/18/2000	Gale E. Smith	674506-2035.2	1236

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EXAMINER	
SRIVASTAVA, KAILASH C	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/484,886	SMITH ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *96-124* is/are pending in the application.

4a) Of the above claim(s) *117-124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *96-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Request for continued examination (i.e., RCE) under 37 CFR §1.114, including the fee set forth in 37 CFR §1.17(e), was filed in this application on April 21, 2004 after a Final action mailed September 24, 2003. Since this application is eligible for continued examination under 37 CFR §1.114, and the fee set forth in 37 CFR §1.17(e) has been timely paid, the finality of the previous Office action mailed September 24, 2003 has been withdrawn pursuant to 37 CFR §1.114. Applicant's submission filed on April 21, 2004 has been entered. Accordingly an RCE has been established and the action on RCE follows.

2. Applicants' Declaration under 37 CFR §1.131 filed March 24, 2004 is acknowledged and entered.

CLAIMS STATUS

3. Claims 96-124 are pending.

4. Claims 96-98 have been amended.

5. Claims 117-124 have been previously withdrawn for the reasons of record at Page 2, item 3 of the Office Action mailed September 24, 2003. Examiner suggests that the non-elected claims cited *supra* be canceled in response to this Office action to expedite prosecution.

6. Claims 96-116 are pending and are examined on Merits.

Objection To Specification

7. 35 U.S.C. §112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is objected to because Example 9 is incompletely written. Appropriate correction is required. Applicants are warned to exercise caution that no new matter is added while revising the application for corrections to completely disclose said Example 9.

The lengthy specification has not been thoroughly checked to determine the presence of all possible minor errors. Applicant s ' cooperation is requested in correcting any errors in the specification of which applicants may become aware.

Claim Rejections Under 35 U.S.C. § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and

process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 96-116 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

From the record of the present written disclosure, the specification, only demonstrates that the claimed composition comprising >95% pure, homogeneous recombinant erythropoietin produced by a baculovirus expression system in cultured insect cells has the claimed (See Page 4, Lines 15-21 of incomplete Example 9 per Amendment and response filed December 17, 2002). However, said description lacks all the steps to produce applicants' claimed >95% pure, homogeneous recombinant erythropoietin produced by a baculovirus expression system in cultured insect cells has the claimed "in-vivo" activity. The Declaration from Dr. Manon Cox also only demonstrates higher in-vivo activity of the claimed preparation (See, e.g., items 8-13) without detailing how the claimed recombinant erythropoietin produced by a baculovirus expression system in cultured insect cells prepared according to the art-known steps employing the same expression system (i.e., baculovirus expression system) and same insect culture has the claimed "in-vivo" activity (See, e.g., Vas-Cath, Inc., 935 F.2d at 1563-64, 19 USPQ2d at 1117 and MPEP, 2163 [R-1] Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement).

10. Claims 96-116 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a glycosylated, >95% pure, recombinant erythropoietin produced by a baculovirus expression system in a cultured insect cell, wherein said erythropoietin has an "in-vivo" activity between 200,000 U/mg to 500,000 U/mg and said erythropoietin stimulates erythropoiesis.

From the record of the presently filed written disclosure, the specification, while enabling for the purification and "in-vitro" activity between 200,000 U/mg to 500,000 U/mg of a glycosylated, >95% pure, recombinant erythropoietin produced by a baculovirus expression system in a cultured insect cell (See last paragraph of incomplete Example 9 at Page 5, Amendment and response filed December 17, 2002) does not reasonably provide evidence of the claimed in-vivo erythropoietic activity of said recombinant erythropoietin either in a cultured cell or in an intact animal. Furthermore, the examples in the specification do not demonstrate in-vivo activity of the composition claimed in the present invention. A

person of skill would not be able to practice the invention because undue experimentation will be required to obtain the erythropoiesis activity cited *supra* due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Undue experimentation will be necessary because there is no recited guidance, i.e., all the steps to obtain a recombinant erythropoietin having an "in-vivo" activity through a baculovirus expression system in cultured insect cells have not been recited in the claimed invention.

11. Claims 96-116 are rejected under 35 U.S.C.§ 112, first paragraph, because the claimed composition does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

From the record of the present written disclosure, the scope of the claimed invention recited in claims 96-97 and 99-116 is not supported by the specification on record because in said specification there are a number of examples (Examples 1-8) showing high density growth of a variety of animal cells (e.g., CHO and *Spodoptra frugiperda* SF900+ insect cells). However, said specification does not show an example demonstrating erythropoietic activity in a cultured cell system or in an intact animal. Based on the description provided in the specification, a person of ordinary skill would not be able to practice the invention because undue experimentation will be required to practice the invention cited *supra.* Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary to delineate all the steps to obtain a recombinant erythropoietin produced through baculovirus expression system produced in cultured *Spodoptra frugiperda* SF900+ insect cells; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims Rejections Under 35 U.S.C § 102

12. Claims 96-97 and 99-116 stand rejected under 35 U.S.C. j102 (b) as anticipated by Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W. B. Saunders Co., Philadelphia, 1988, Page 581) for the reasons of record in the Office Action mailed March 25,2003.

In response to art rejections under 35 U.S.C.§ 102(b) discussed supra, citing a number of Case laws, applicants argue that Quelle et al. with or without Dorlands do not teach or suggest the instantly claimed invention, because the claimed invention is to an in-vivo activity, wherein said activity is an

element of the presently claimed invention. Applicants, however, quoting Quelle reference recite on record that Quelle et al's purified recombinant erythropoietin has little, if any in vivo activity' (See Applicants' response filed June 25, 2003, Page 11, Lines 29-30).

Applicants' above arguments regarding the rejections to Claims 96-97 and 99-116 have been fully considered but are not persuasive for the reasons of record on Page 4, item 9 in Office Action mailed March 25, 2003 and in item 5 on Pages 2-3 of the Office Action mailed September 23, 2003. Furthermore, nowhere in any of the Claims 96-97 and 99-116 applicants have claimed "in-vivo" activity for said >95% pure, homogeneous recombinant erythropoietin produced by a baculovirus expression system in cultured insect cells. Only place that applicants assert that their recombinant erythropoietin stimulates erythropoiesis is at Page 4, Lines 15-21 of incompletely written Example 9 (See Page 5, Amendment and response filed December 17, 2002). However, even in that assertion applicants have not demonstrated in-vivo activity of their recombinant erythropoietin in a cultured animal cell or in an intact animal. Applicant also assert in above cited paragraph that in contrast to all recombinant erythropoietins reported in prior art literature that applicants have cited, applicants' recombinant protein obtained in same way (i.e., expressed in baculovirus vector, wherein said baculovirus is cultivated in insect culture and subsequently said recombinant erythropoietin is purified) as prior literature is different than those from cited literature. Despite the fact that Dr. Manon Cox has exemplified vis. a vis. in-vivo activity of the instantly claimed recombinant erythropoietin/ (s) from said prior art literature (e.g., Quelle et al., Blood. 1989. Volume 74, Pgs. 652-657), said declaration does not disclose distinctiveness either during preparation or in properties of said erythropoietin vis. a vis. recombinant erythropoietin described in prior art literature. Since said distinctiveness is key to the instantly claimed invention, applicants are requested to disclose under 35 U.S.C. § 132, said distinct production step/property of the claimed recombinant erythropoietin vis. a vis. at least one recombinant eehropoietin (e.g., one that Quelle et al. have reported, since that erythropoietin is closest to the applicants' claimed erythropoietin). In absence of requested data/information, the examiner-cited prior art deems to anticipate the instantly claimed invention.

Claims Rejections Under 35 U.S.C §103(a)

13. Claims 96-116 stand rejected under 35 U.S.C. § 103(a) as obvious over Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W.B. Saunders Co., Philadelphia, 1988, Page 581) for the reasons of record in the Office Action mailed March 25, 2003.

In response to the rejections to Claims 96-116 in the Office Action mailed March 25, 2003, applicants argue that the claimed invention is unobvious over the cited reference, because the cited reference does not disclose, teach, incite or suggest, or provide motivation to arrive at the presently

claimed invention. This argument is not deemed to be persuasive because of the reasons of record and discussion presented above. Additionally, Quelle et al teach a similar product prepared in the manner and having same range of purity (i.e., 200,000 U/mg to 500,000 U/mg) as recited in the claimed invention, the product would intrinsically function in the same, or essentially the same manner as in the claimed invention. Instantly claimed higher purity of said eryhropoietin is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter, which is well within the purview of the skilled artisan. Therefore, the product disclosed in the prior at reference would intrinsically stimulate erythropoiesis even with "limited in vivo activity".

CONCLUSION

14. No Claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (571) 272-0926 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Art Unit 1651
(571) 272-0923

June 6, 2004

RALPH GITOMER
PRIMARY EXAMINER
GROUP 1200